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## FIG. 1A

```
agggagaggc agtgaccatg aaggctgtgc tgcttgccct gttgatggca
  51 ggcttggccc tgcagccagg cactgccctg ctgtgctact cctgcaaagc
 101 · ccaggtgagc aacgaggact gcctgcaggt ggagaactgc acccagctgg
      gggagcagtg ctggaccgcg cgcatccgcg cagttggcct cctgaccgtc
 151
      atcagcaaag gctgcagctt gaactgcgtg gatgactcac aggactacta
 201
      cgtgggcaag aagaacatca cgtgctgtga caccgacttg tgcaacgcca
 251
      gcggggccca tgccctgcag ccggctgccg ccatccttgc gctgctccct
 301
      gcactcggcc tgctgctctg gggacccggc cagctatagg ctctgggggg
 351
      ccccgctgca gcccacactg ggtgtggtgc cccaggcctt tgtgccactc
 401
      ctcacagaac ctggcccagt gggagcctgt cctggttcct gaggcacatc
 451
      ctaacgcaag tttgaccatg tatgtttgca ccccttttcc ccnaaccctg
 501
     accttcccat gggccttttc caggattccn accnggcaga tcagttttag
551
     tganacanat ccgcntgcag atggcccctc caaccntttn tgttgntgtt
601
     tccatggccc agcattttcc accettaacc ctgtgttcag gcacttnttc
651
     ccccaggaag ccttccctgc ccaccccatt tatgaattga gccaggtttg
70.1
     gtccgtggtg tcccccgcac ccagcagggg acaggcaatc aggagggccc
751
     agtaaaggct gagatgaagt ggactgagta gaactggagg acaagagttg
801
     acgtgagttc ctgggagttt ccagagatgg ggcctggagg cctggaggaa
851
     ggggccaggc ctcacatttg tggggntccc gaatggcagc ctgagcacag
901
     cgtaggccct taataaacac ctgttggata agccaaaaaa aaaaaaaa
951
```

### FIG. 1B

MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQV ENCTQLGEQCWTARIRAVGLLTVISKGCSLNCVDDS QDYYVGKKNITCCDTDLCNASGAHALQPAAAILALLPAL GLLLWGPGQL

# FIG. 2

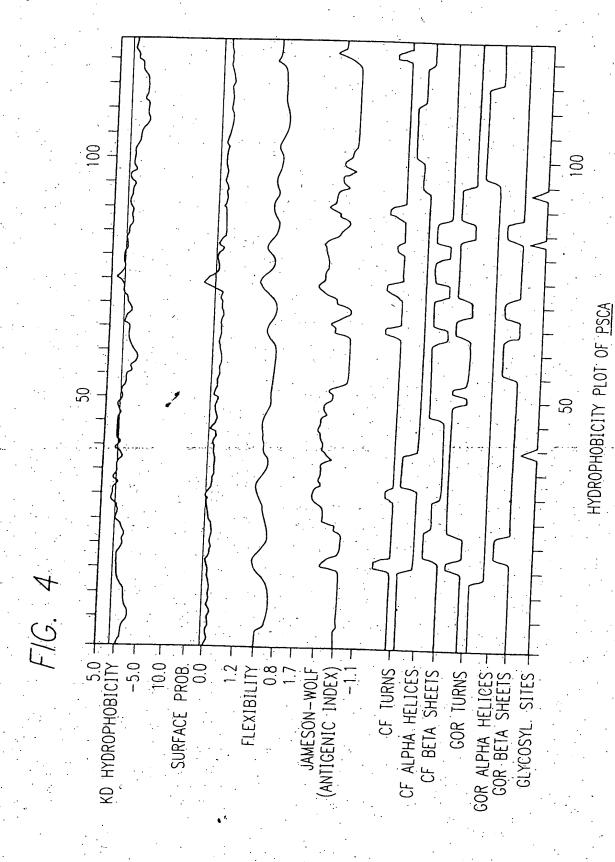
. •	1	ATGAAGACAGTTTTTTTTATCCTGCTGGCCACCTACTTAGCCCTGCATCCAGGTGCTGCT																									
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		C1	GC	AG	TG	CT.	ATT	ГС	A T.G	CA	CAG	CA	CA	GAT	GA.	ACA	AC	AG	AG/	CT	GTC	TGA.	ATG	TAC	AGA	4AC	
61		GA	CG	TC												rgt				GA	CAGA	CT:	+ TAC	ATG	TCT	+ FTG	1,2
		L	·Q		С	Y	S		С	T	Α	(	<b>)</b> .	М	N	N		R	D	С	, F,	N	V	Q	N	I	
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121		AC	GT(	CGO	SA	ССТ	GG	TC	GTO	STC	AAC	GA	AΑ	TG	TAG	CGC	G	TAC	GC	CCG	GTA	ACC	TGA	\GC/	·	-+ GT	18
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51		K P P T T L G L L T V L C S L L L W G S AGCCGTCTGTAGGCTCTGGGAGAGCCTGCAC																									
	TC	GG	CAG	ίΑC	:A1	СС	GA(	GA:		CTC	TCG	GA	TG	+- GT/	TC	GGG	СТ	-+- AA	CA	 CTT	CCC	+ TAC	TCG	ACG	+ GTG	42	Ó
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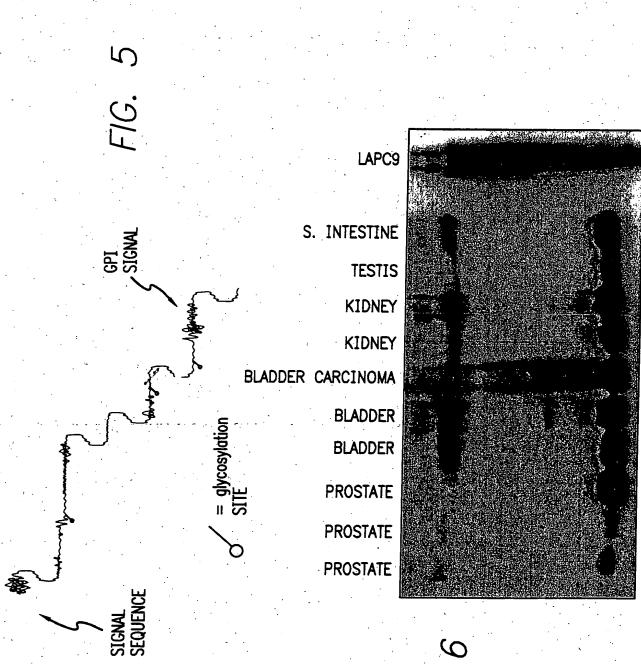
# FIG. 3

```
MKIFLPVLLAALLGVERASS
   MKAVLLALLMAGLALOPGTA
   MKTVLFLLATYLALHPGAA
 21 LMCFS CLNQKS,N*LYCLKPTI
 21 LLCYSCKAOVSN*EDCLQVEN*
 21 LQCYSCTAQMNN*RDCLNVQN*
61 VTFGHSLSKTCSPACPIPEG
  V - - - - - I S K G C S L N C V D D S Q V - - - - - I S K G C S S Q C E D D S E
61
81 VNVGVASMGISCCQSFLCN*F
76 DYYVGKK-N*ITCCDTDLCN*A
76 NYYLGKK-N*ITCCYSDLCN*V
101 S A A D G G L R A S V T L L G A G L L L
95 S.GAHALOPAAAILALLPALG
95 NGAHTLKPPTTLGLLTVLCS
121 SLLPALLRFGP
115 C L L W G P G Q L - -
```

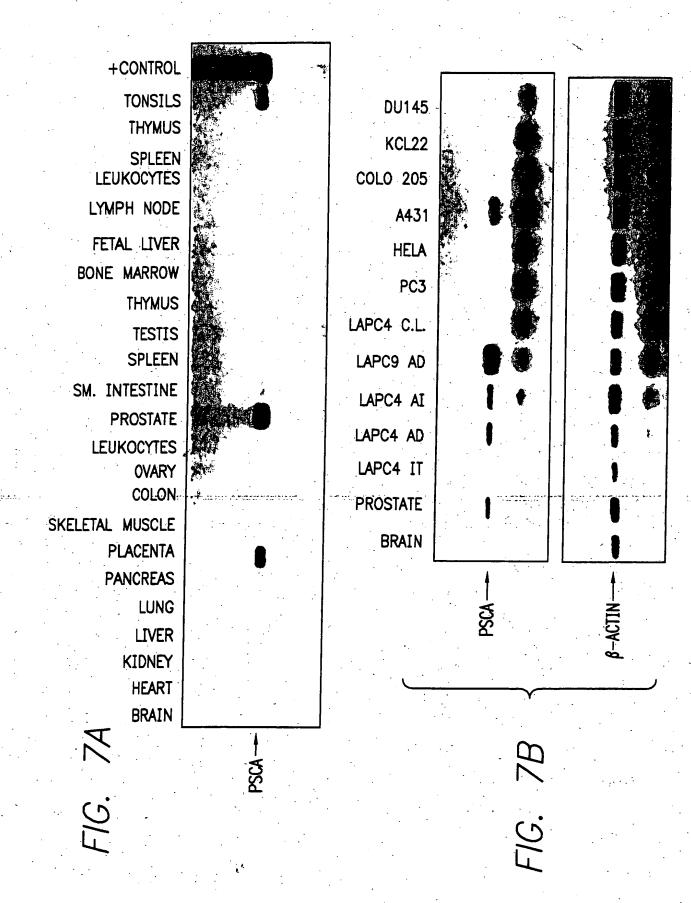
115 L L L W G S S R L - -

**hPSCA** 





F/G. 6



F/G. 84

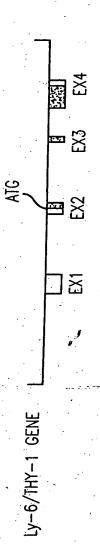


FIG. 8B

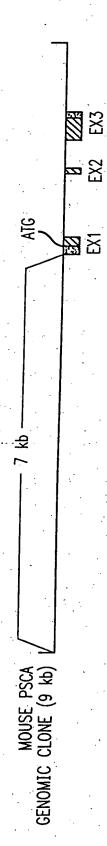
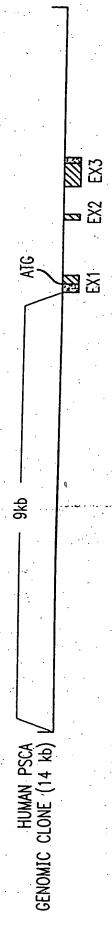
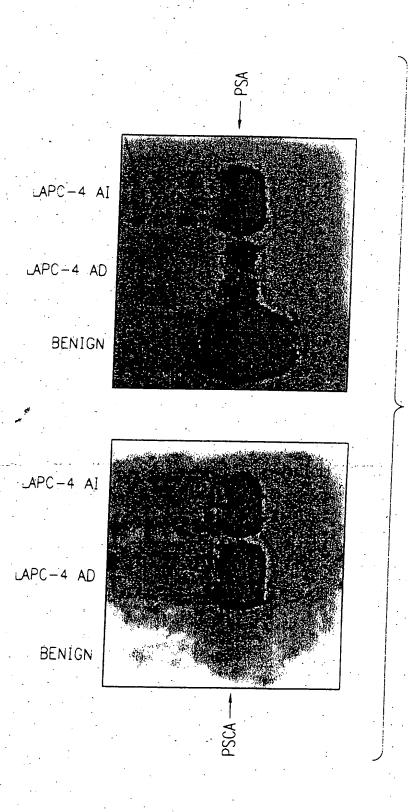
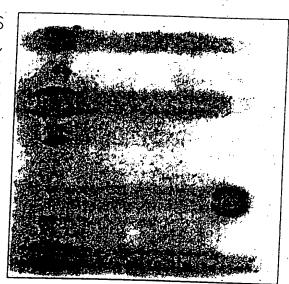


FIG. 8C





PANCREAS
KIDNEY
SKELETAL MUSCLE
LIVER
LUNG
PLACENTA
BRAIN
HEART



PERIPHERAL LEUKOCYTES

COLON

SMALL INTESTINE

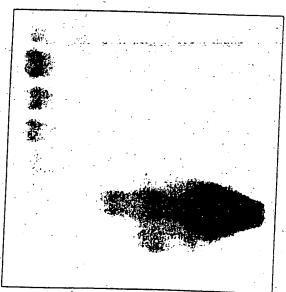
OVARY

TESTIS

PROSTATE

THYMUS

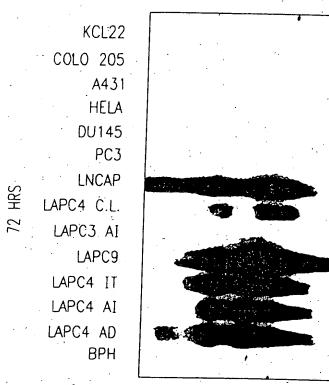
SPLEEN



KCL22 COLO 205 DU145 LNCAP LAPC4: C.L. LAPC3 AI LAPC9 LAPC4 IT LAPC4 AI LAPC4 AD

COLO 205 A431 HELA DU145 PC3 LNCAP LAPC4 C.L. LAPC3 AI ~LAPC9 LAPC4 IT LAPC4 AI LAPC4 AD BPH.

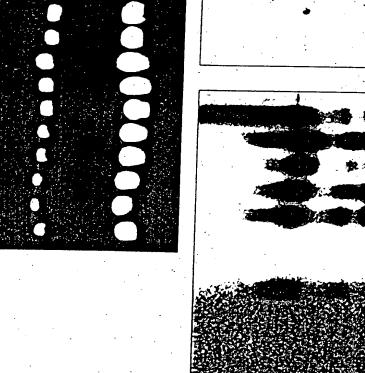
7G. 10B



KCL22
COLO 205
A431
HELA
DU145
PC3
LNCAP
LAPC4 C.L.
LAPC3 AI
LAPC9
LAPC4 II
LAPC4 AI
LAPC4 AD

.PSM

BPH



BPH

LAPC4 AD

LAPC4 AT

LAPC3 AT

LAPC4 C.L.

LAPC4 C.L.

LAPC4 C.L.

LAPC4 C.L.

LAPC4 C.L.

LAPC3 AT

LAPC4 C.L.

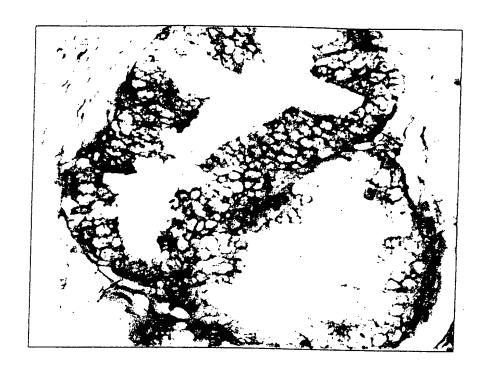
LAPC3 AT

LAPC3 AT

LAPC4 C.L.

LAPC6 TI

FIG. 11A



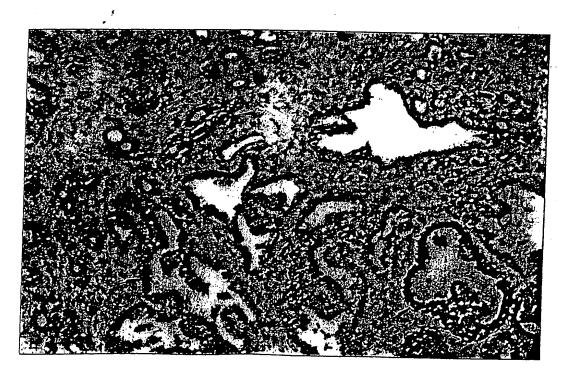
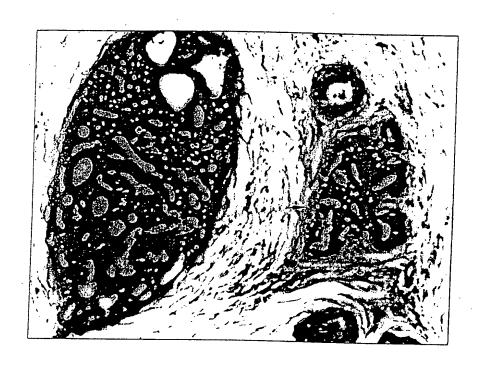
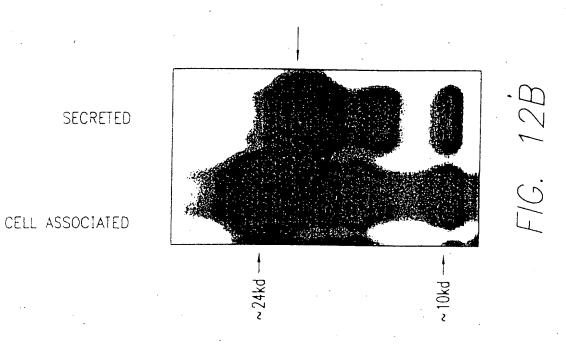


FIG. 11B



F/G. 11C

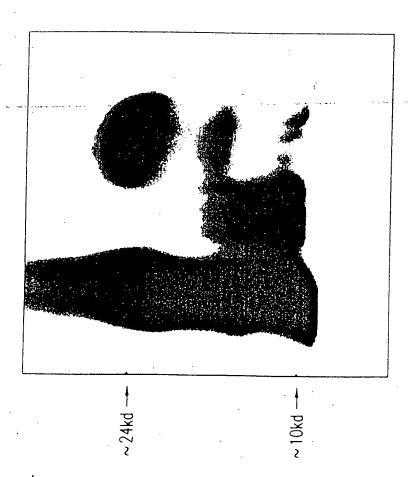


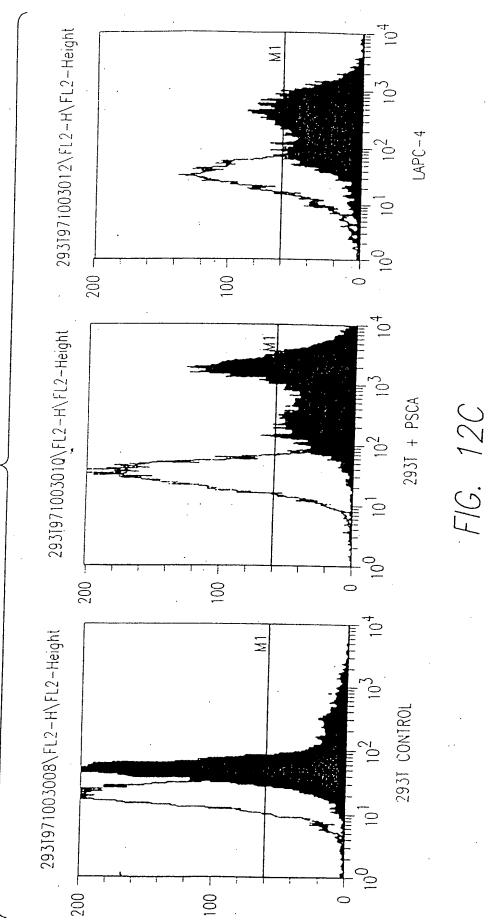
O GLYCOSIDASE

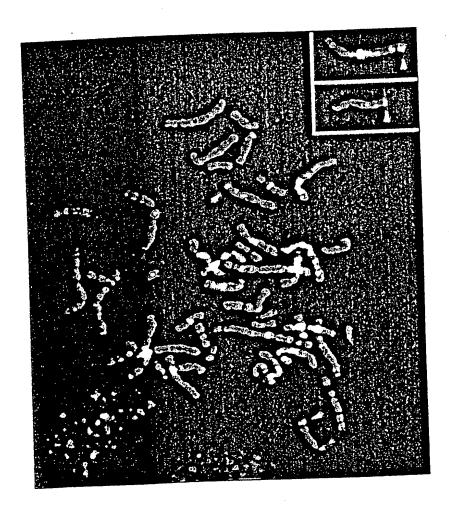
N GLYCOSIDASE F

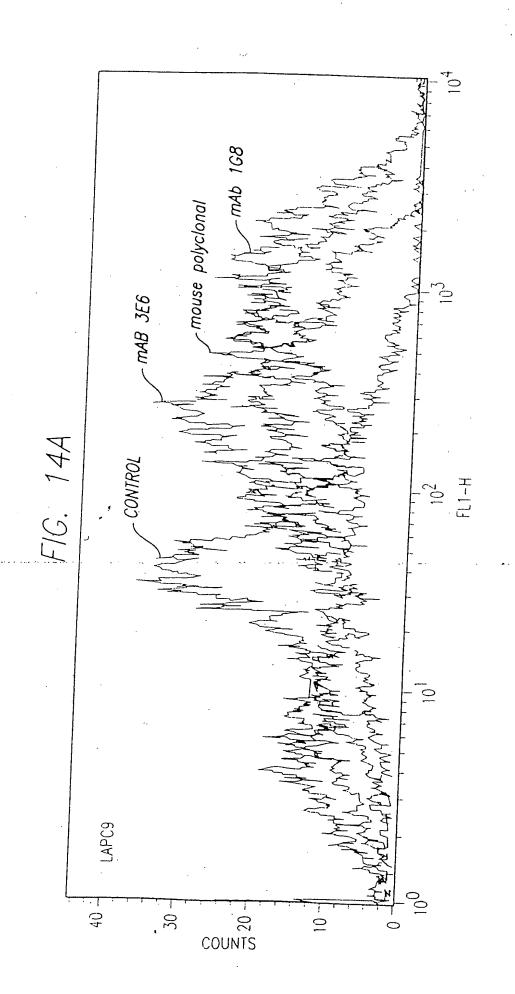
CONTROL

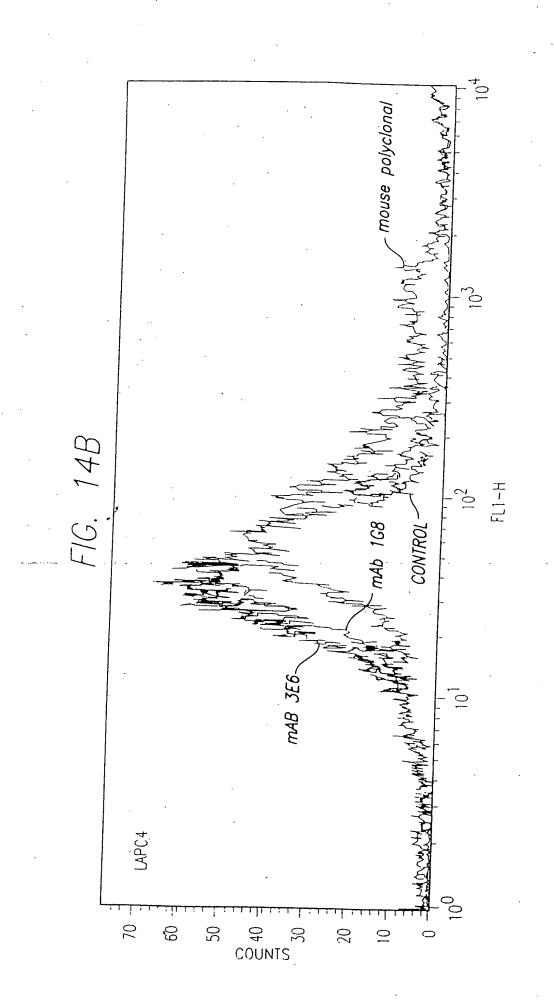
5. 12











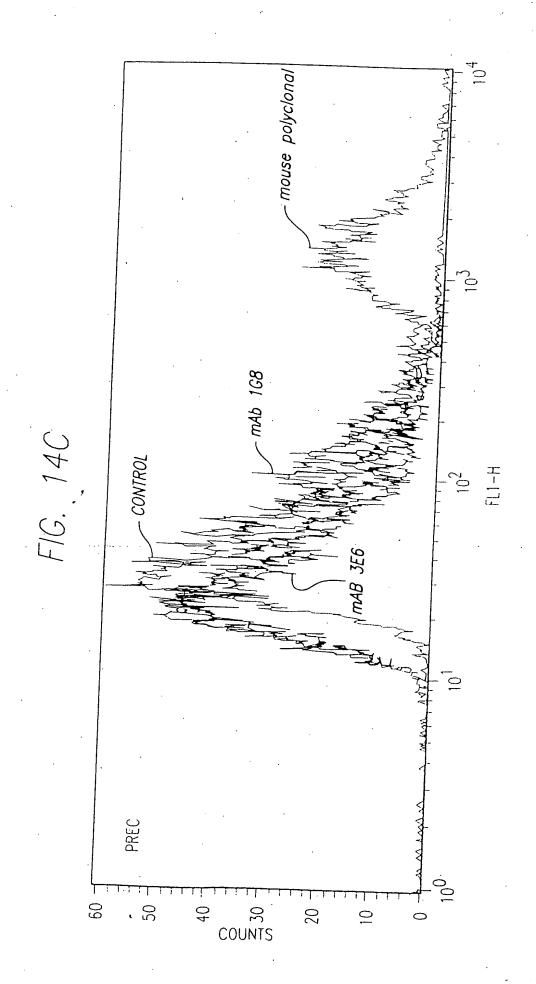


FIG. 15B

hSCA-2 hPSCA mPSCA			·			
A S S h	P T V O E IN	2 J >	P C C	G N* F C N* A V V	A S C L	·
GVER ANDR	> Q Q Z	S A G 1 R A V B R A I G	ONA ONA ONA ONA ONA ONA ONA ONA ONA ONA	0 S F F F F F F F F F F F F F F F F F F	A IC P C	
CAALE MAGE	O X X SS IN X X X X X X X X X X X X X X X X X X	VFVSA WTAR	TCSP GCSL GCSS S		A A I C	O
P V		0 N Y C C C C C C C C C C C C C C C C C C	N H H	A S M G	G G L R A L C K R A L C K R A L C K R B P	S S R R
W K A V	M CO F		7 F G H	7 9 7 N N N N N N N N N N N N N N N N N	S A B D N S S A H A H A H A H A H A H A H A H A H	SEET PA
<del></del>	21	4 4 4	61	81 76 76	95	121

## PROSTATE STEM CELL ANTIGEN (PSCA) IS A GPI-ANCHORED PROTEIN

. 37

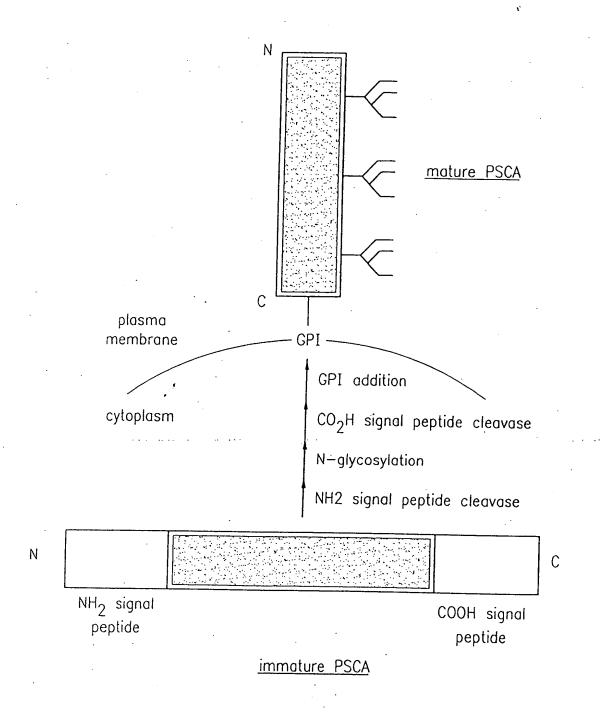


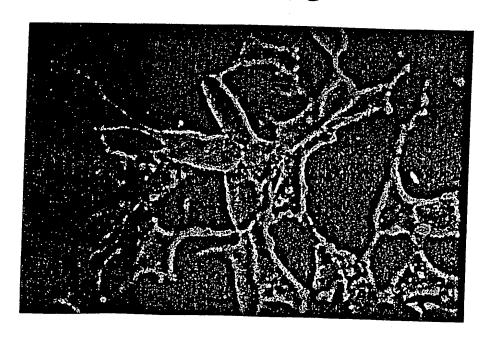
FIG. 16B

FIG. 17

# FISH ANALYSIS OF PSCA AND 3-myc IN PROSTATE CANCER

#34 c-myc #75 c-myc #75 PSCA

FIG. 18



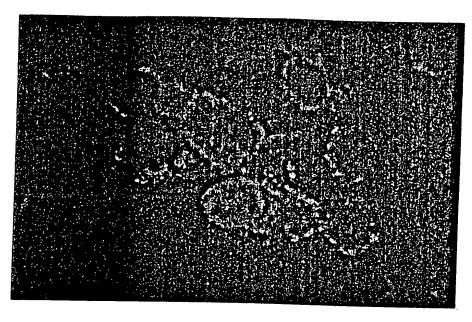
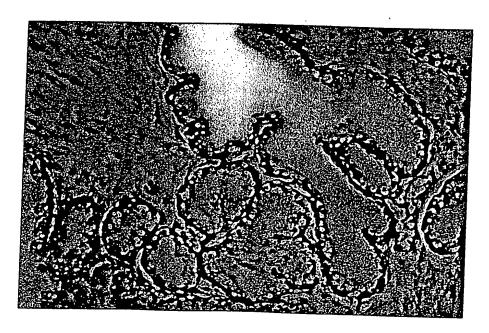


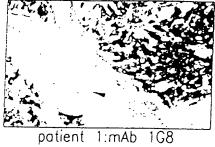
FIG. 19

FIG. 20



# FIG. 2.1

## PSCA IMMUNOSTAINING OF PRIMARY TUMORS





patient 2:mAb 1G8



patient 3:mAb 1G8



patient 4:mAb 3E6

# FIG. 22

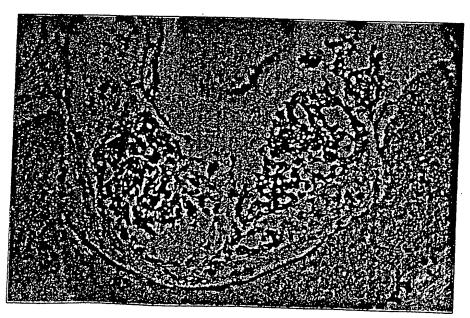
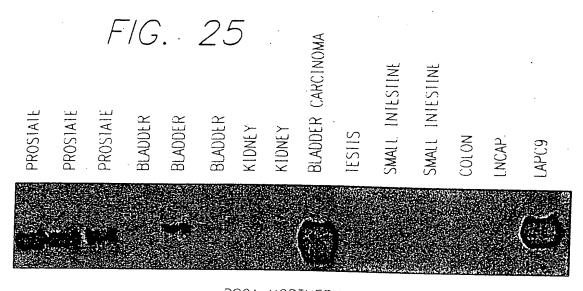




FIG. 23

FIG. 24





PSCA NORTHERN

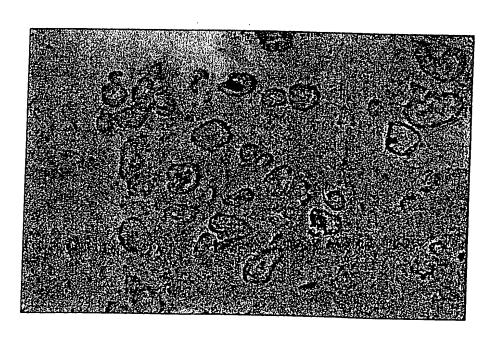


FIG. 26

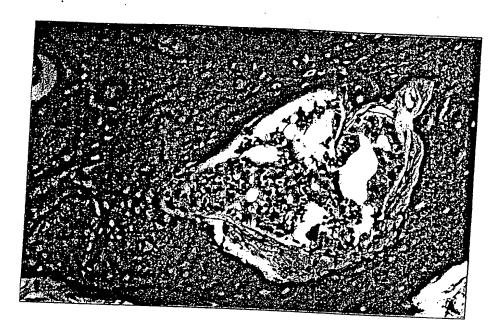
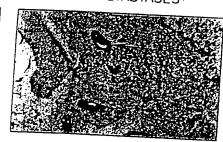


FIG. 27

# PSCA IMMUNOSTAINING OF BONY METASTASES





Patient 5: H and E. and mAb 1G8





Patient 4: H and E and mAb 3E6

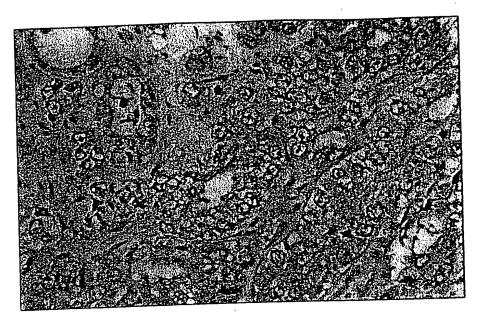
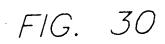


FIG. 29





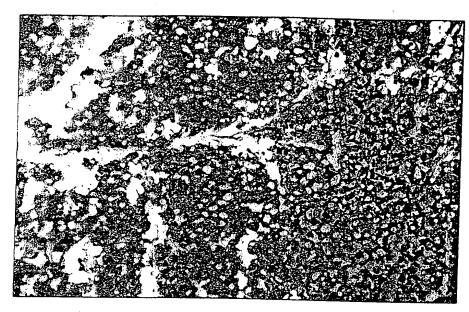


FIG. 31

FIG. 32

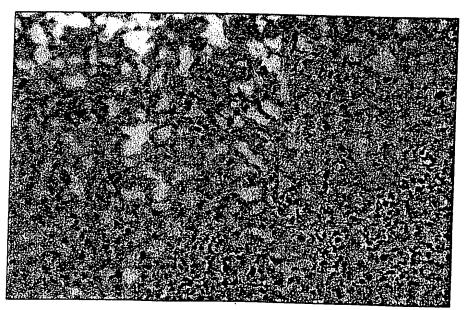
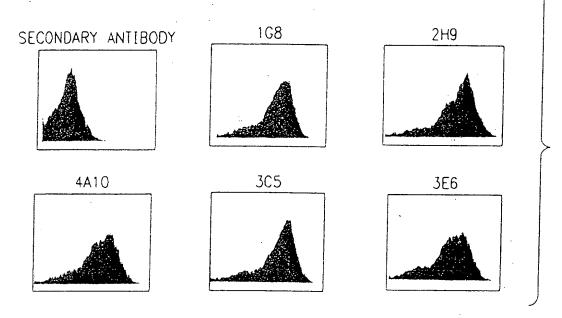


FIG. 33

#### PSCA EXPRESSION IN LAPC-9 XENOGRAFT BY FACS



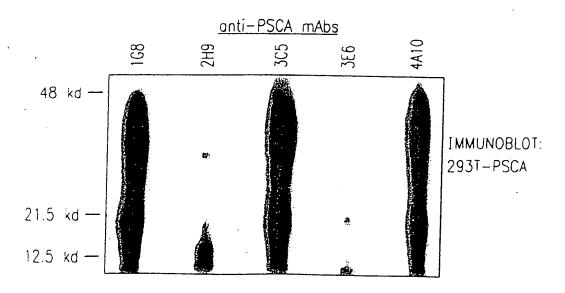
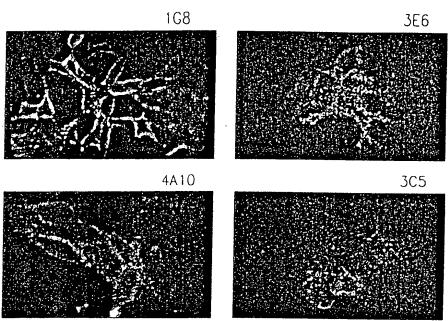


FIG. 34

FIG. 35

IMMUNOFLUORESCENT STAINING OF LNCOP-PSCA CELLS



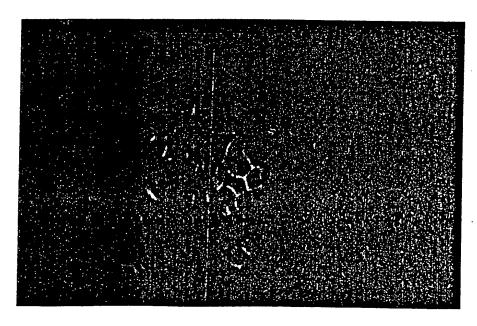
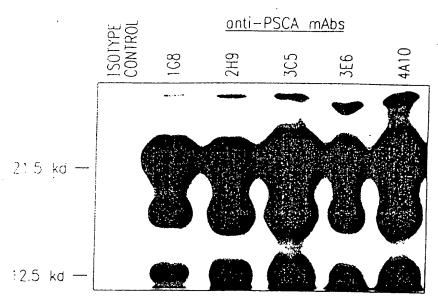
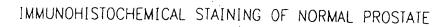


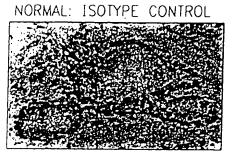
FIG. 36

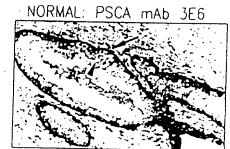


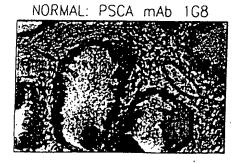
IMMUNOPRECIPITATION: 293T-PSCA

FIG. 37









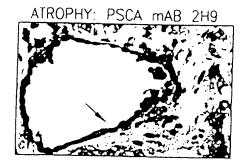
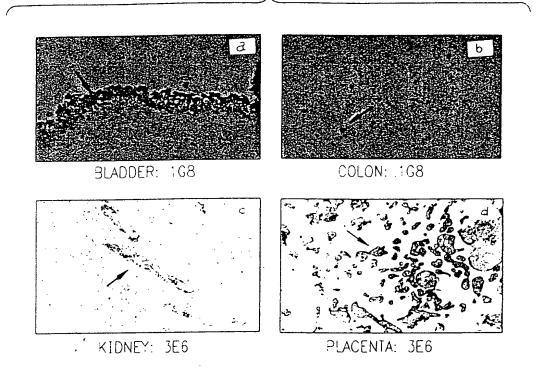


FIG. 38

# FIG. 39A



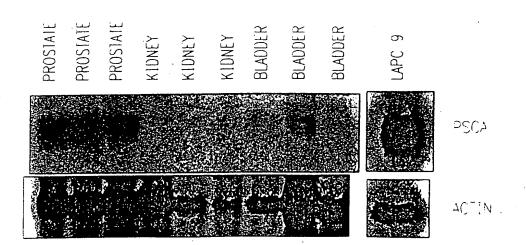
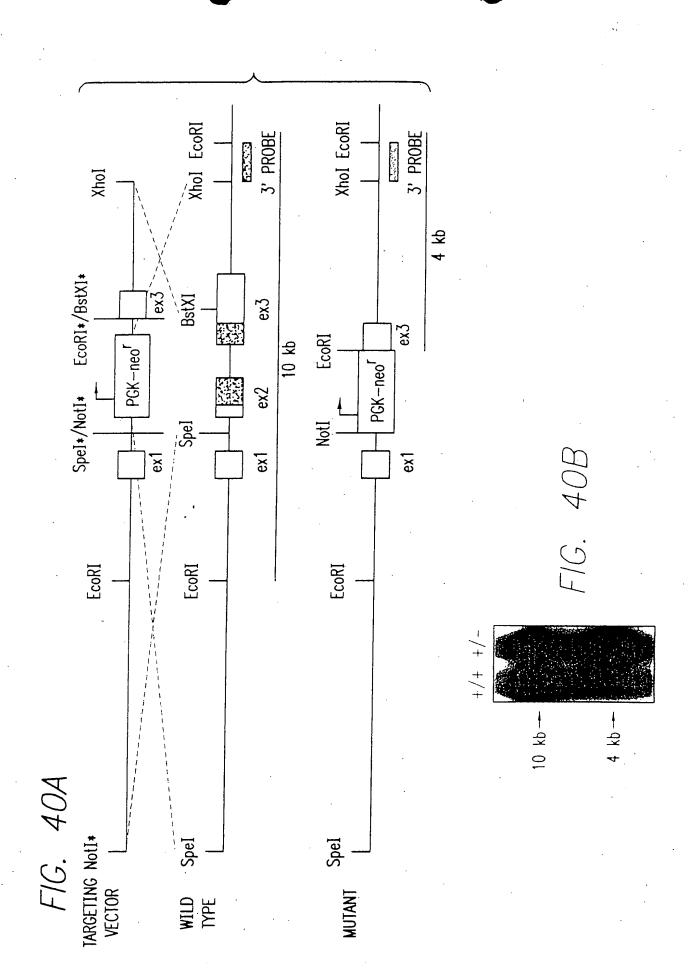


FIG. 39B



MOUSE BEARING PROSTATE CANCER	CHARACTERISTICS	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCICINOMA 28 WKS	NO METASTASES	LOW-GRADE PIN 5-8 WKS HIGH-GRADE PIN 8-12 WKS	INVASIVE CARCICINOMA 12 WKS METASTASES IN LYMPH NODE LING LIVED AND DOLL	COLO, LIVEN AND BONE
	TARGET TISSUES	PROSIAIE (SECRETORY CELLS) URETHRAL, MAMMARY AND SWEAT GLAND	PROSTATE (SECRETARY OFFICE	CELLS)		
	C3(1) (-3 kh)/	SV40 LARGE+SMALL, T MAROULAKOU et al. 1994 PNAS	PROBASIN (-426 bp)/	SV40 LARGE+SMALL, T GREENBERG et al	1995 PNAS	

LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCICINOMA 16 WKS METASTASES IN LYMPH NODE, LUNG, LIVER, AND BONE

(NEUROENDOCRINE CELLS)

PROSTATE

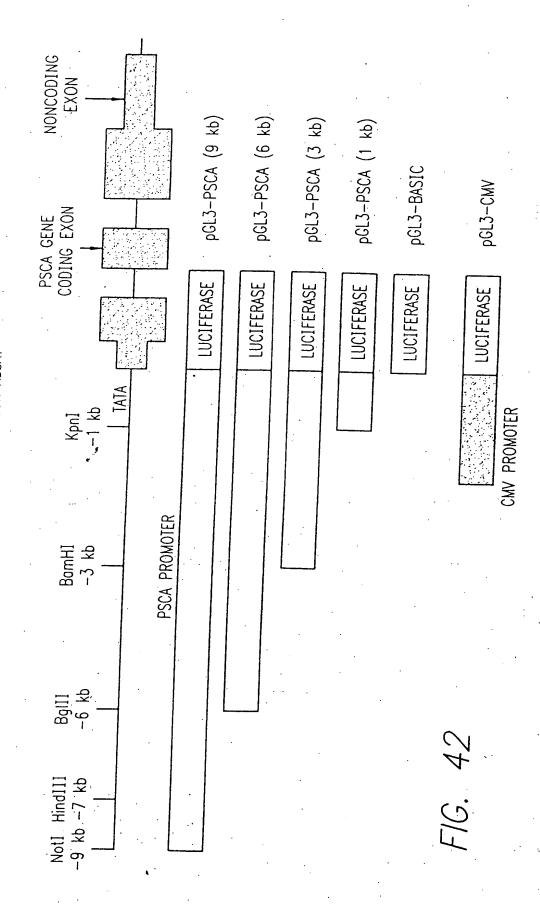
CRYPIDIN2 (-6.5 kb), SV40 LARGE+SMALL, T

CARABEDIAN et al.

1998 PNAS

SMALL INTESTINE

REPORTER GENE CONSTRUCTS FOR TRANSFECTION ASSAY



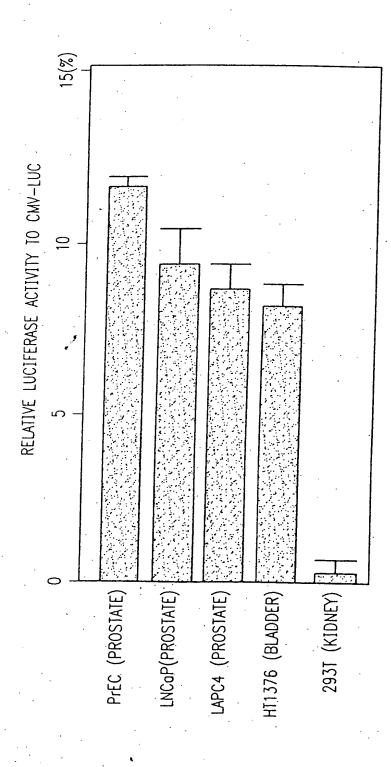


FIG. 43

IDENTIFICATION OF PROSTATE—SPECIFIC ELEMENTS WITHIN PSCA PROMOTER SEQUENCES

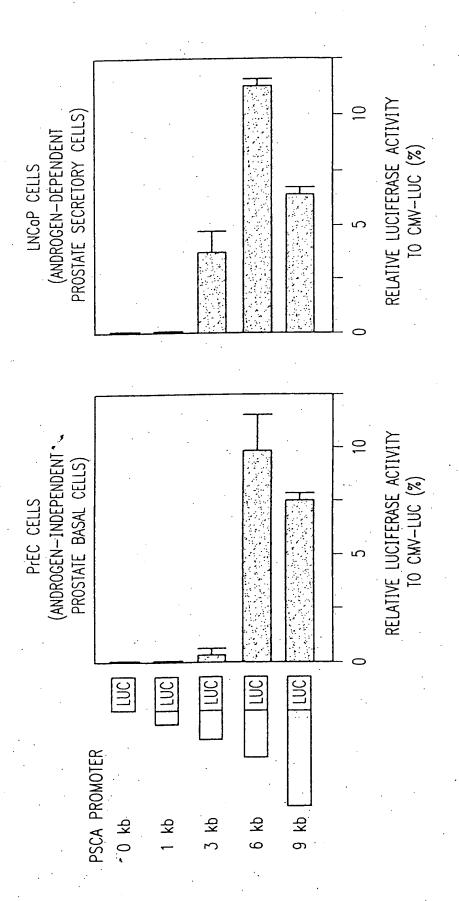


FIG. 44

(DNA POSITIVE) NUMBER OF FOUNDERS EXON 3 EXON 2 INTRON INTRON 3'hGH 3.hGH 0FP INTRON INTRON - EXON 1 <u>د</u> ATG GENOMIC STRUCTURE OF PSCA PSCA PROMOTER (6kb) PSCA PROMOTER (9kb) PSCA PROMOTER (9kb) PSCA PROMOTER (6Kb) PSCA PROMOTER (9kb) PSCA PROMOTER (6Kb) PSCA PROMOTER PSCA(9 kb)-GFP-3'hGH PSCA(6 kb)-GFP-3'hGH PSCA(6 kb)-SV40TAG PSCA(9 kb)-SV40TAG PSCA(9 kb)-GFP PSCA(6 kb)-GFP

UPDATE OF TRANSGENIC MOUSE PROJECTS

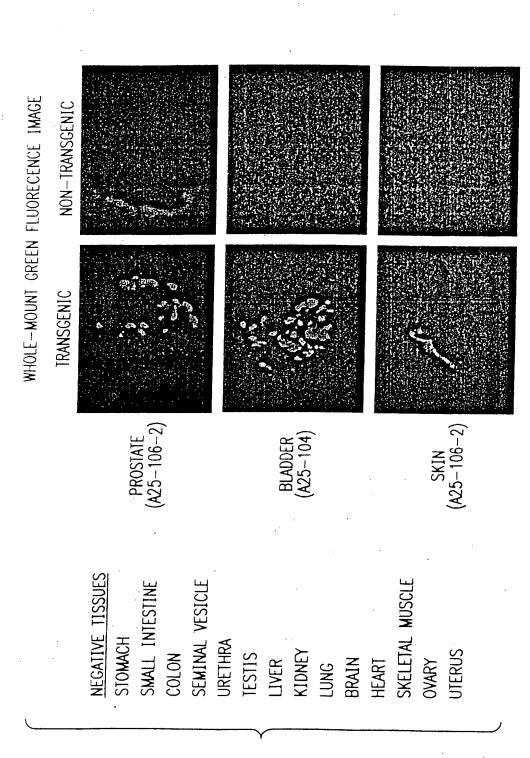
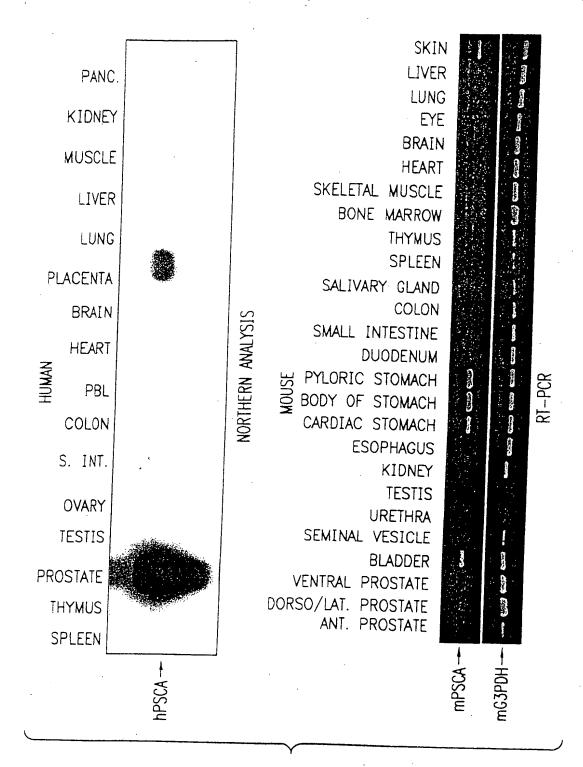
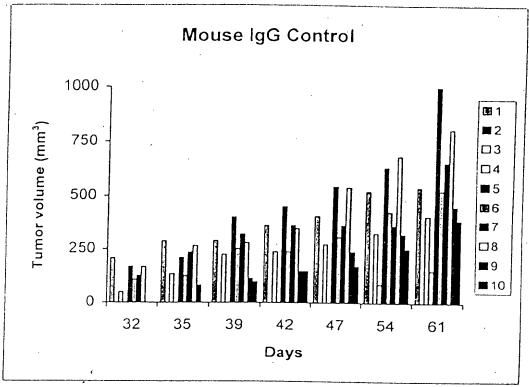


FIG. 46



F1G. 4



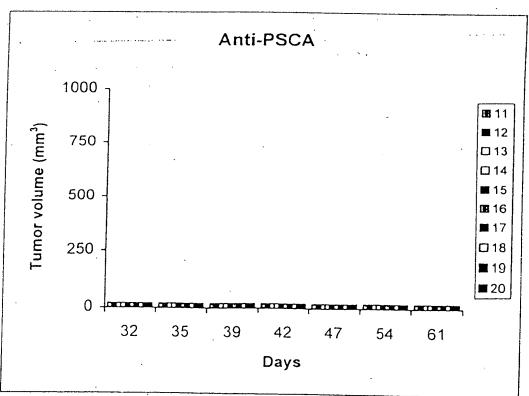
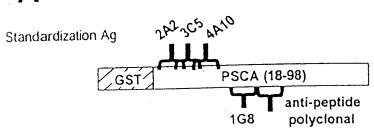


FIG. 50

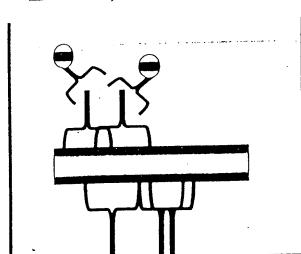
A



Engineered mammalian secreted form

		 	12.5
lg leader.	DCCA /40 00\	LANV	C HIS
i lo leader i	PSCA (18-98)	/MI I	C I TIO
10.00 To 70.00		 -	N. S.

B



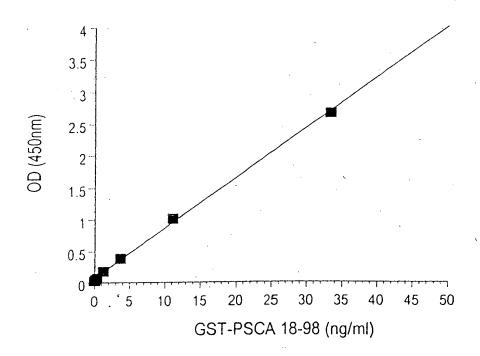
Anti-IgG2a HRP

Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)

**PSCA** 

Affinity purified anti-peptide polyclonal + mAb 1G8 (IgG1)

A



B

Sample	OD+range (n=2)	ng/ml
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

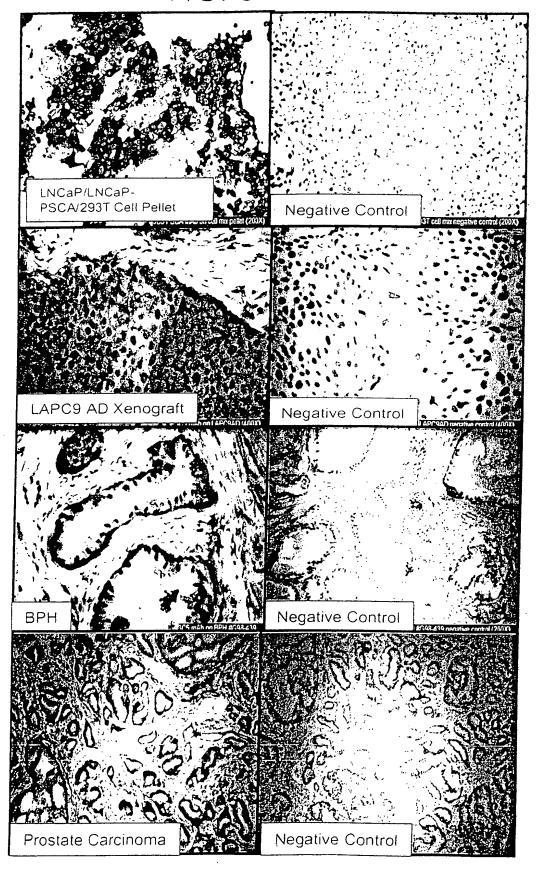
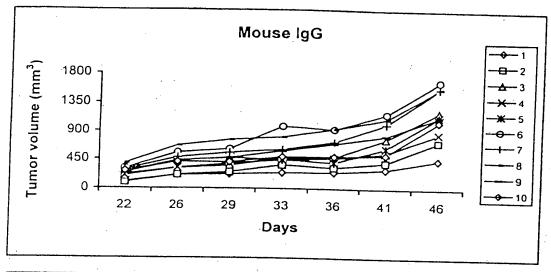
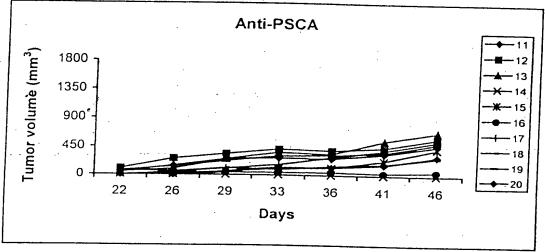


FIG. 53





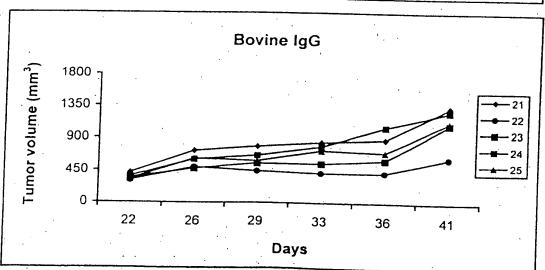
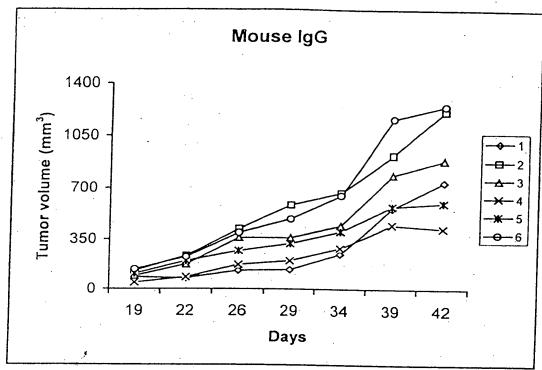


FIG. 54



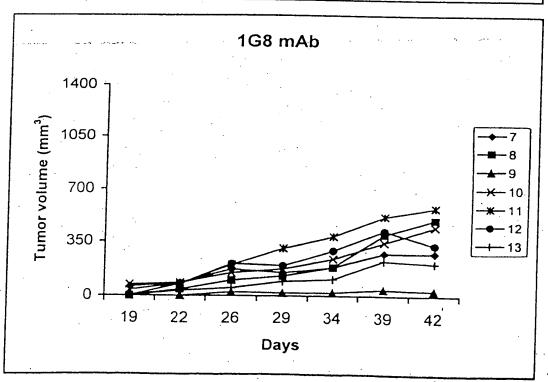
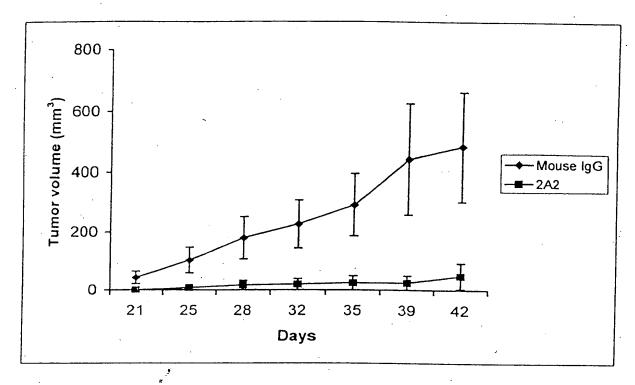


FIG. 55



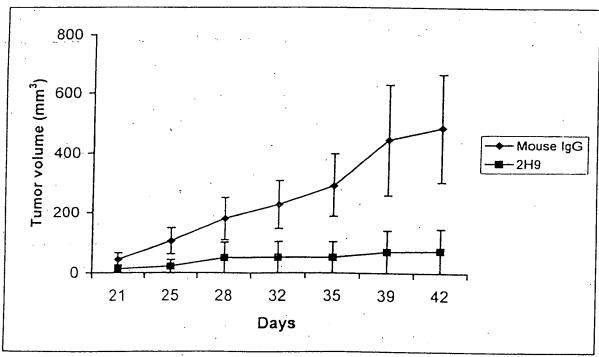
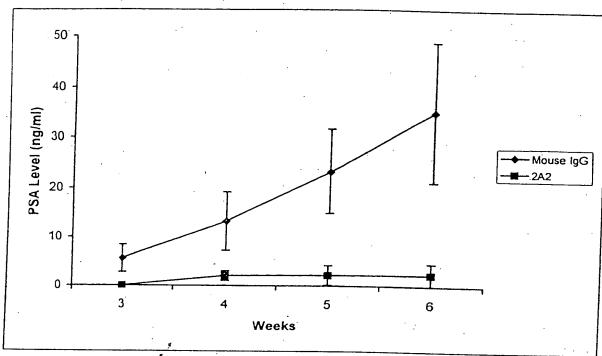


FIG. 56



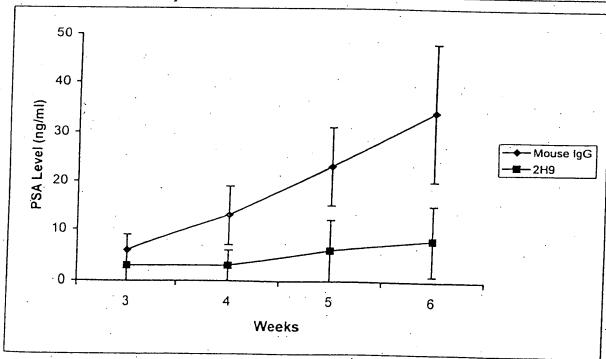
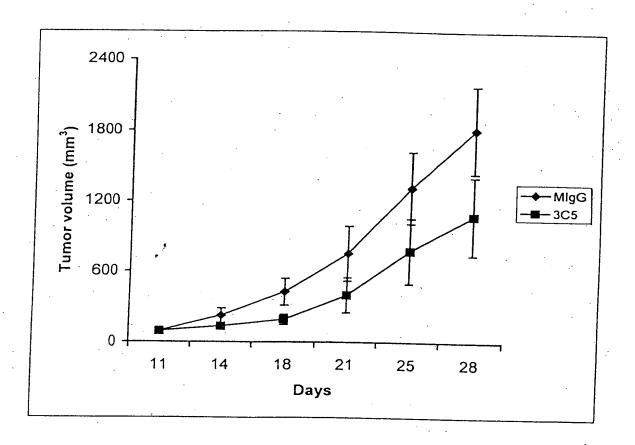


FIG. 57



### FIG. 58

9 TGCTTCTTCCTGATGGCAGTGGTTATAGGAGTCAATTCAGAGGTTCAGCTGCAGCAGTCT <u>۸</u> æ I Ž

GGGGGAGAACTTGTGAGGTCAGGGGCCTCAGTCAAGTTGTCCTGCACAGCTTCTGGCTTC 120 Ļ Ś Þ ග

09 AACATTAAAGACTACTATATACACTGGGTGAATCAGAGGCCTGACCAGGGCCTGGAGTGG 180 Сij Ö ø Ω بم æ o z - CDR1 z

ATTGGATGGATTGATCCTGAGAATGGTGACACTGAATTTGTCCCGAAGTTCCAGGGCAAG 240 ଠା CDR2 -Ö ග

GCCACTATGACTGCAGACATTTTCTCCAACACAGCCTACCTGCACCTCAGCAGCCTGACA 300 ഗ 二 Ц Z ഗ Σ

TCTGAAGACACTGCCGTCTATTACTGTAAAACGGGGGGTTTCTGGGGCCAAGGGACTCTG 360 120 T CDR3 -S K

GTCACTGTCTGCAGCCAAACGACACCCCCATCTGTCTATCCACTG

TTGGTAGCAACAGCCTCAGATGTCCACTCCCAGGTCCAACTGCAGCAACCTGGGTCTGAA α α 'n, 二

CTGGTGAGGCCTGGAACTTCAGTGAAGCTGTCCTGCAAGGCTTCTGGCTATACATTCTCC 120 ß Ы × ഗ

180 AGCTACTGGATGCACTGGGTGAAGCAGAGGCCTGGACAAGGCCTTGAGTGGATTGGAAAT හ 团 ග O Σ

ATTGACCCTGGTAGTGGTTACACTAACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240 Z CDR2 U

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300 Н ഗ ß ഗ

360 TCTGCAGTCTATTACTGTACAAGCCGATCTACTATGATTACGACGGGATTTGCTTACTGG CDR3 E

160 GGCCAAGGGACTCTGGTCTCTGCAGCTACAACAACAGCCCCATCTGTCTATCCA 420

CTGGCC

AATGACTTCGGGTTGAGCTGGGTTTTTATTATTGTTCTTTTAAAAGGGGTCCGGAGTGAA

GTGAGGCTTGAGGAGTCTGGAGGCTGGTGCAACCTGGAGGATCCATGAAACTCTCC 120 ტ ტ O ග Ġ ტ Ы

TGTGTAGCCTCTGGATTTACTTTCAGTAATTACTGGATGACTTGGGTCCGCCAGTCTCCA 180 ഗ CDR1

80 GAGAAGGGGCTTGAGTGGGTTGCTGAAATTCGATTGAGATCTGAAAATTATGCAACACAT 240 Y N æ Ш

100 TATGCGGAGTCTGTGAAAGGGAAATTCACCATCTCAAGAGATGATTCCAGAAGTCGTCTC 300 Ŋ ß ₽ ୯୬ 臼

TACCTGCAAATGAACAACTTAAGACCTGAAGACAGTGGAATTTATTACTGTACAGATGGT 360 E-4 ഗ ×

CTGGGACGACCTAACTGGGGCCAAGGGACTCTGGTCACTGTCTCTGCAGCCAAAACGACA 420 140 Λ . 1 

#### FIG. 61

#### CDR1 Comparisons

1G8	$1gG_{1k}$	Middle	G	F	NI	K	D	YY	I	н
2H9	$1gG_{1k}$	N-Term.	G	F	T F	s	N	YW	M	1 T
4A10	1gG <sub>2ak</sub>	N-Term.	G	Y	T F	s	s	Y W	M	н

#### CDR2 Comparisons

1G8	$lgG_{ik}$	WIDPENGDTEFVPKFQG	
2H9	1gG <sub>1k</sub>	EIRLRSENYATHYAESVK	G
4A10	1gG <sub>2ak</sub>	NIDPGSGYTN YAENIK	

#### CDR3 Comparisons

1G8	$1gG_{ik}$		G	F							
2H9	1gG <sub>1k</sub>	L	G	R	P	Ñ	a ingo to was no <del>di uta</del> na di ti				
4A10	1gG <sub>2ak</sub>	R	s	$\mathbf{T}$	M	IT	T G	F	Α	Y	

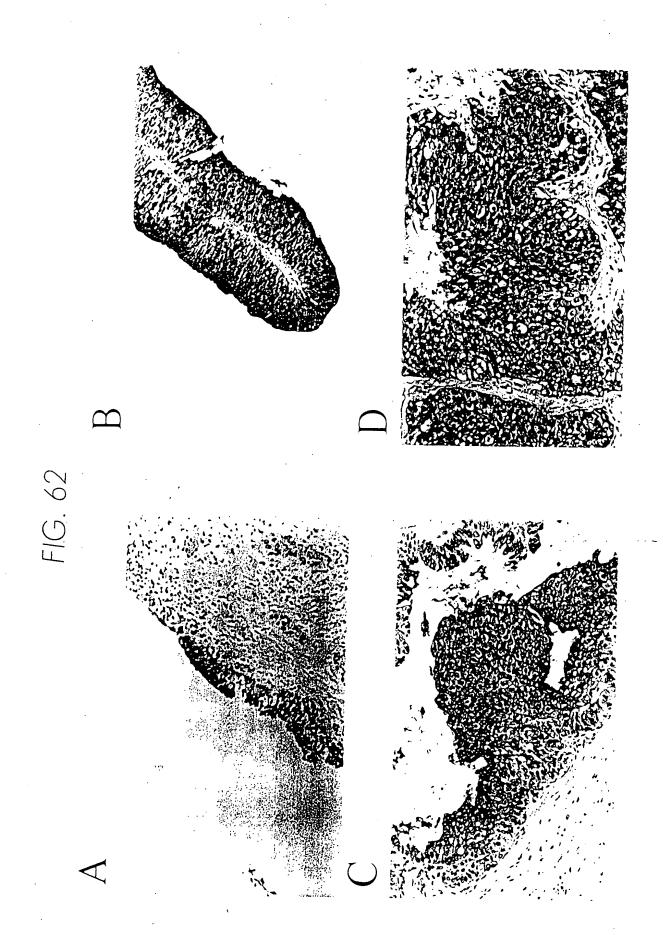


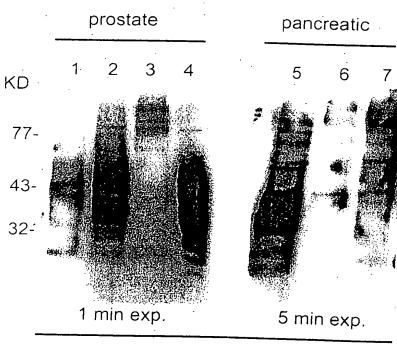
FIG. 63

		prostate						pan	creat	tic
kb 9.0-	1	2	3	4	5		6	7	8	9
4.4-		٠								
2.4-		•		ينون او د او د د د د د د د د د د د د د د د د د د						
1.4-					P					

- 1. Prostate
- 2. LAPC-4 AD
- 3. LAPC-4 AI
- 4. LAPC-9 AD 5. LAPC-9 AI
- 6. PANC-1 7. BxPC-3 8. HPAC

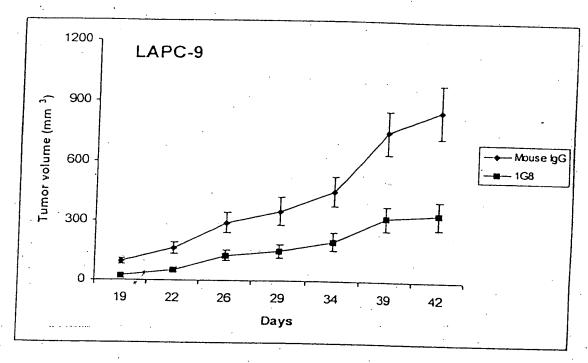
- 9. Capan-1

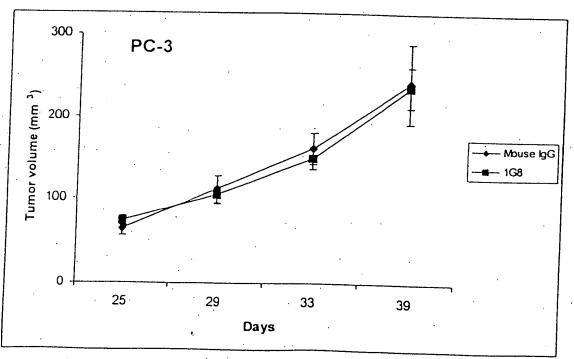
FIG. 64



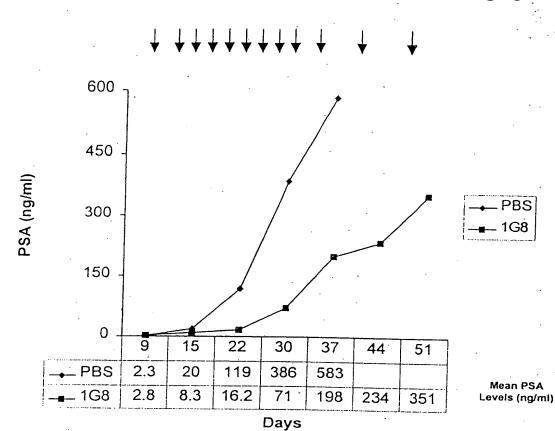
#### anti-1G8

- 1. LAPC-4 AD
- 2. LAPC-9 AI
- 3. LNCaP
- 4. LNCaP-PSCA
- 5. HPAC
- 6. Capan-1 7. ASPC-1



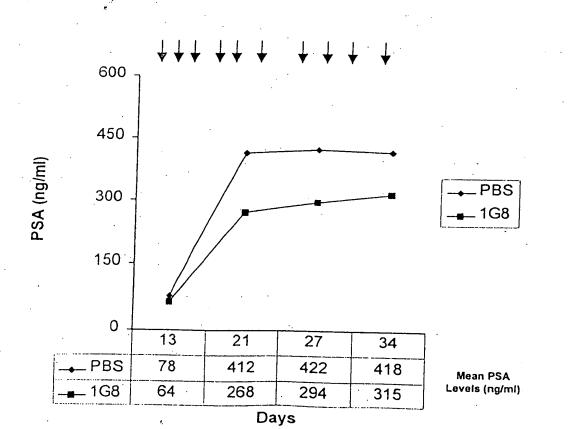


F1G. 66



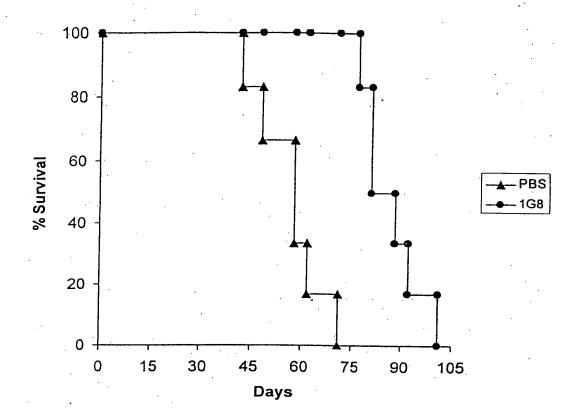
A)

B)

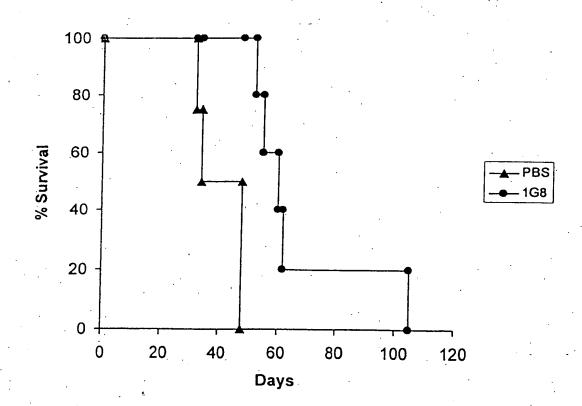


F1G. 67

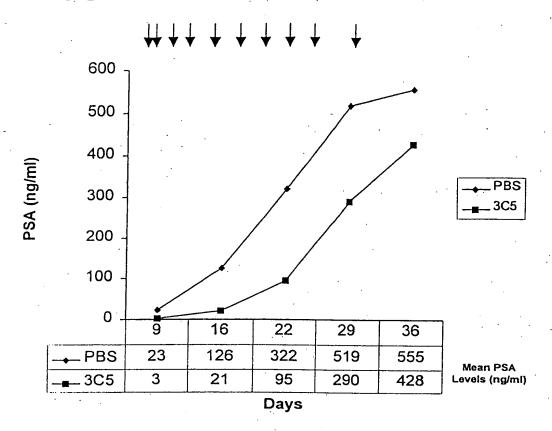




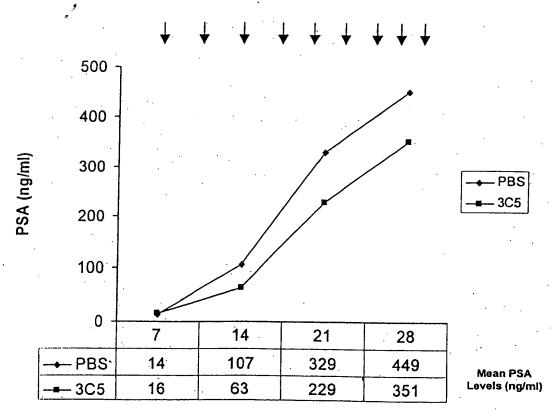
B)



A)

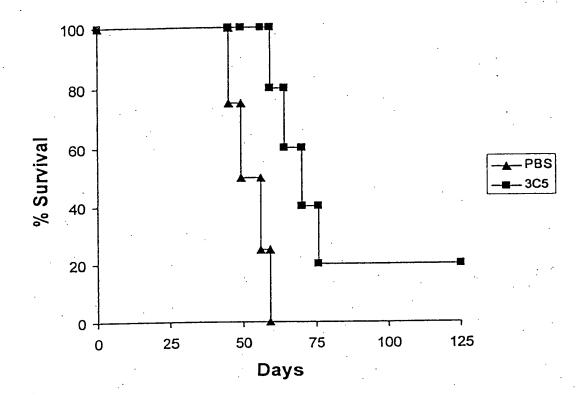


B)

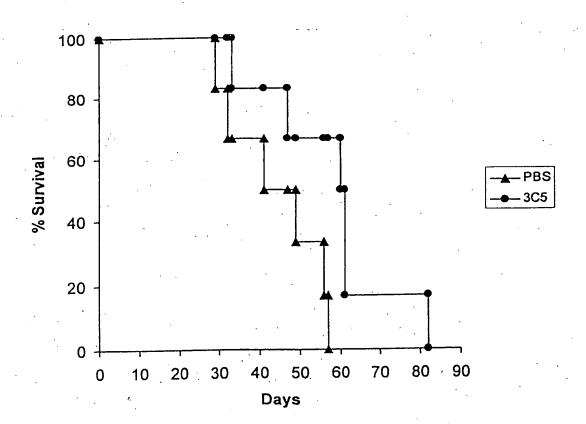


Days

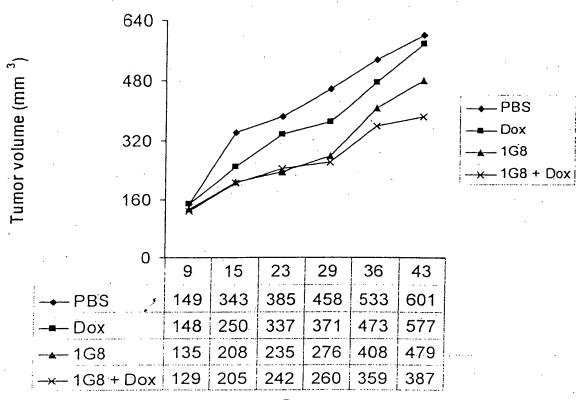




#### B)

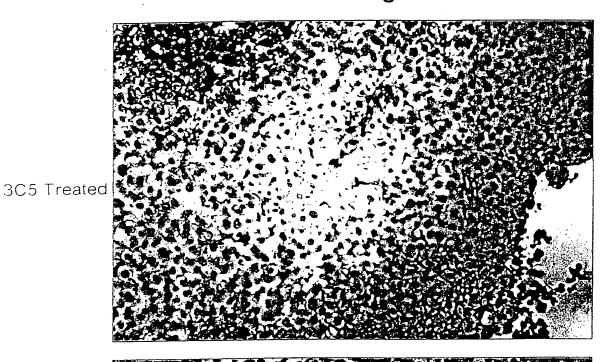


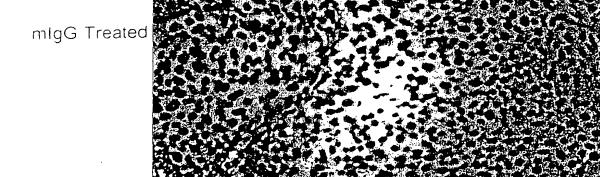




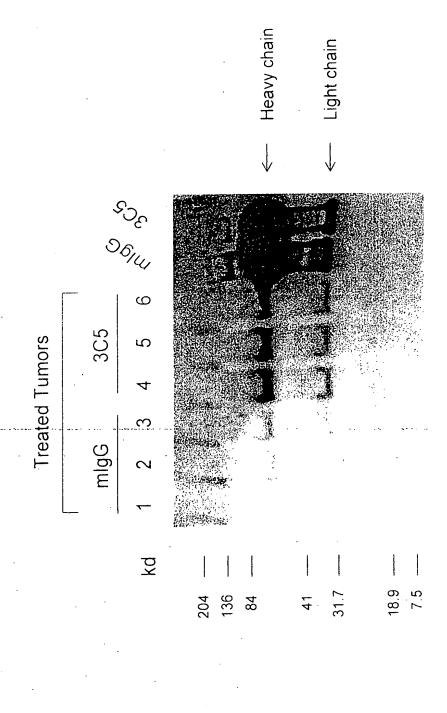
Days

FIG. 71
PSCA 3C5 MAb Localizes within LAPC9AD Xenograft Tissue





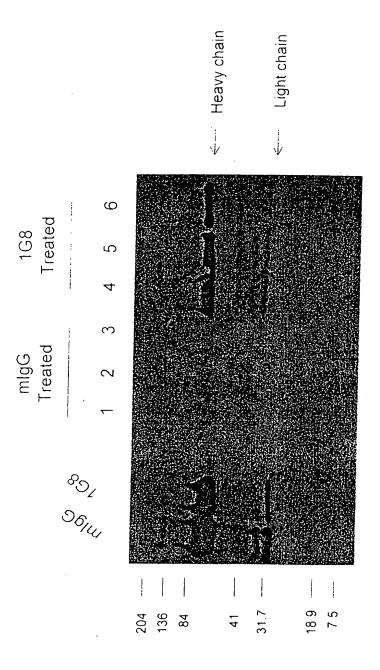
## 3C5 Anti-PSCA MAb is Localized to Established **LAPC-9 Tumors**



Western blot developed with  $\alpha$ -mlgG/k

FIG. 72

# SPECIFIC TARGETING OF THE 1G8 ANTI-PSCA MAD TO ESTABLISHED LAPC-9 TUMORS



- x-MlgG Western

Method: Mice bearing established LAPC-9 tumors (>100 mm<sup>3</sup>) were injected with either mlgG or the anti-PSCA MAb 1G8 Tumors were harvested a week later and made into protein lysates for Western analysis